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PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 07333208	A2	19951222	JP 1994-150549	19940608

OTHER SOURCE(S): MARPAT 124:205804

AB Spherical substances obtained by **sol**-gel process, where acidic solns. are added to Q[M(OR')3]2 (I) or its mixts. with Si(OR)4 (II) (R, R' = alkyl; Q = (CH2)n, .PHI., .PHI.2; .PHI. = divalent benzene ring; M = Si, Ti, Zr), are claimed. Spherical column packings are obtained by using SiO2-based powders as cores, adding I and optionally II to the cores, adding acidic solns., and coating of the resulting products.

L9 ANSWER 15 OF 19 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1995:641521 CAPLUS
DOCUMENT NUMBER: 123:63536
TITLE: Alkylene-bridged polysilsesquioxane aerogels: highly porous hybrid organic-inorganic materials
AUTHOR(S): Loy, Douglas A.; Jamison, Gregory M.; Baugher, Brigitta M.; Russick, Edward M.; Assink, Roger A.; Prabakar, S.; Shea, Kenneth J.
CORPORATE SOURCE: Properties of Organic Materials Department, Sandia National Laboratories, Albuquerque, NM, 87185-1407, USA
SOURCE: J. Non-Cryst. Solids (1995), 186, 44-53
CODEN: JNCSBJ; ISSN: 0022-3093
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Alkylene-bridged polysilsesquioxane gels were prepd. by **sol**-gel polymns. of .alpha.,.omega.-bis(triethoxysilyl)alkanes. The gels were extd. with supercrit. carbon dioxide to afford a novel class of hybrid org.-inorg. aerogels. The effect of the length of the alkylene bridging group and catalyst (HCl and NaOH) on the structure was examd. The mol. structure was characterized by solid-state 13C and 29Si cross polarization magic angle spinning NMR spectroscopy. The alkylene bridging groups survived **sol**-gel polymn. to give materials with av. degrees of condensation of 79 and 90% for the acid- and base-catalyzed aerogels, resp. SEM was used to examine the macroscopic structure of the gels and nitrogen sorption porosimetry was used to measure their surface areas and pore structures. Most of the alkylene-bridged aerogels were mesoporous, high-surface-area materials. As with alkylene-bridged polysilsesquioxane xerogels, the surface area decreased with increasing alkylene bridging group length. Only the base-catalyzed tetradecylene-bridged aerogel was found to be non-porous.

L9 ANSWER 16 OF 19 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1993:450456 CAPLUS
DOCUMENT NUMBER: 119:50456
TITLE: Alkylene-bridged silsesquioxane **sol**-gel synthesis and xerogel characterization. Molecular requirements for porosity
AUTHOR(S): Oviatt, Henry W., Jr.; Shea, Kenneth J.; Small, James H.
CORPORATE SOURCE: Dep. Chem., Univ. California, Irvine, CA, 92717, USA
SOURCE: Chem. Mater. (1993), 5(7), 943-50
CODEN: CMATEX; ISSN: 0897-4756
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Alkylene-bridged silsesquioxane xerogels with alkylene spacers spanning the range from ethylene to tetradecamethylene were synthesized. Hydrolysis and condensation conditions using 1 N HCl in THF or 1 N NaOH in

PATENT ABSTRACTS OF JAPAN

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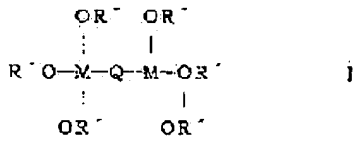
(22)Date of filing : **08.06.1994**

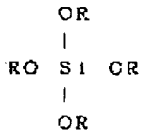
(71)Applicant : **PIATETSUKU KK**
(72)Inventor : **URYU YOSHIAKI**

(54) COLUMN PACKING AGENT FOR LIQUID CHROMATOGRAPHY

(57)Abstract:
PURPOSE: To enable the development of specific separation capacity by using a specific alkoxide silane compd,. having an org. bond as a constitutional component and producing a spherical packing agent by a sol-gel method.
CONSTITUTION: A compd. having a structure represented by formula I [wherein R' is an alkyl group such as -CH3, or -C2H5, Q is a chain alkylene group represented by -(CH2)n-(wherein n is an integer of 1-3) or an aromatic cyclic compd. represented by -ϕ- or -ϕ-ϕ- (wherein ϕ is a divalent benzene ring) and M is one of Si, Ti and Zr] is used. This compd. can be used alone but is generally used along with a compd. represented by formula II (wherein R is an alkyl group such as -CH3 or -C2H5) as a raw material of sol-gel reaction.



I



II

LEGAL STATUS

[Date of request for examination]

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[Kind of final disposal of application other than the examiner's decision of rejection or application converted registration]

[Date of final disposal for application]

[Patent number]

[Date of registration]

[Number of appeal against examiner's decision of rejection]

[Date of requesting appeal against examiner's decision of rejection]

[Date of extinction of right]

* NOTICES *

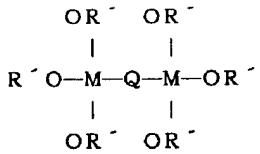
DETAILED DESCRIPTION

[Detailed Description of the Invention]
[0001]
[Field of the Invention] In recent years, in connection with the development with rapid biotechnology, as for liquid chromatography, usefulness is increasing increasingly. If the matter and heat which are especially hard to evaporate are applied, it is going across the applicable field extensively as a refining means of not only research phases, such as an unstable separation of the matter, analysis, and identification operation, but a quality control and production control top and a manufacture. Therefore, in connection with it, the development of the bulking agent with more high separability ability is desired more quickly under a more gradual condition.
[0002]
[Description of the Prior Art] As a column packing material for liquid chromatography, organic polymer systems, such as polystyrene and a polyacrylate, and silica systems, such as silica gel and a porous glass, are known conventionally. It seems that whether it is the column packing material excellent in the polymer system and the silica system throat fence has a fault advantage in each, and which cannot say that it is good. general -- a polymer system -- compression rigidity -- it was low and there was a fault by which deformation is not avoided in the use under the liquid phase hyperbaric pressure On the other hand, a mechanical strength is high, it is possible to fill up a particle with the bottom of the hyperbaric pressure into a column, a polymer system is excelled in resolution and the direction of a silica system has an advantage with the high repeatability of measured value. However, if PH of a mobile phase becomes alkaline, since lysis of parent silica gel will progress quickly, a fault, such as receiving a limit of a service condition, appears. It waited eagerly for the development of the silica system column packing material excellent in alkali resistance in such a background.
[0003] Moreover, the separability ability of a column packing material can control the separability ability of the column by changing a positive (negative) polarity or a parent (non-dense) aquosity. [in / it shall be based on the difference of the residence time in the column resulting from compatibility by the polarity etc. or rebounding nature of the adsorption-and-desorption ability between the front face (stationary phase) of a bulking agent, and a dissociated compound (separation object), or both etc., and / a stationary-phase front face]
[0004]
[Problem(s) to be Solved by the Invention] For obtaining a more highly efficient column packing material, in addition to a high thing, separability ability must be physically [chemically in physical properties, and] stable, and has influence to the life of a column with this big. For example, although the bulking agent with which the mechanical strength had both stable advantage over large PH domain like a polymer system like a silica system that it is high and there is little intumescence deflation has a desirable property, it can be called one.
[0005] However, it sets in such a conventional silica system. (1) Since many things are the letters of spallation, it wants for the pack density to a column to have a difficulty in rose ****** repeatability, to change this into a spherical particle, and to raise repeatability, (2) There is a fault with low silica system [pure] alkali resistance, and some want to improve this, (3) The quality of the material of a bulking agent (stationary phase) itself or its front face is reformed, the polarity and hydrophobic property are embellished, it has been the technical probrem of enhancement of the bulking agent of a silica system to enable it to want to be able to give more various separability ability etc., and this application also makes this etc. the technical probrem.
[0006]
[Means for Solving the Problem] Some manufacturing methods by the sol-gel method which used the metal alkoxide as the raw material are reported as a means for raising alkali resistance in glass and a ceramic field now. Although it is not practical as a liquid chromatography bulking agent, the report of a zirconia system bulking agent excellent in alkali resistance is also reported (notes: reference reference).
[0007] However, since the configuration of bulking agents, such as this, is a letter of spallation, if density nonuniformity arises when a column is filled up with this, variation arises in the repeatability of the most important measured value by the aspect ratio of fine particles and it is not much practical, it is not [that there is nothing] powerful. Having the property which was excellent in alkali resistance with an application of a sol-gel method, he developed the column packing material of the shape of a true sphere which restoration nonuniformity does not produce, obtained the good result, and the invention-in-this-application person applied previously. (Japanese Patent Application No. 56725 [six to])
[0008] Although the invention in this application made the same invention and the technical probrem concerning previous

application, it was able to apply a means to obtain the bulking agent of the shape of a true sphere by the sol-gel method by the technique developed in previous invention as the means, and was able to obtain the column packing material which has the larger characteristic feature in separability ability by new completion of technique which introduces a special hydrophobic group into the mainframe quality of the material of the bulking agent, and its front face. The manufacture of the bulking agent with these various characteristic features was able to use the raw material which has the special structure described minutely below, and was able to attain it by manufacturing a spherical-packing agent with a sol-gel method with a means like point **.

[0009] The raw material which has special structure here is **** about the compound which has the structure shown in the next (** 1).

[化1]

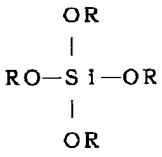


inside [of a formula], and R' -- ** -- CH3 and ** C2 H5 etc. -- alkyl group;Q -- (**) -- it is expressed with the chain type alkylene machine expressed with ** (CH2) n ** or (b) **phi**, and ** phi-phi ** -- aromatic -- cyclic-compound;M is 1 in Si, Ti, and Zr ((phi expresses the divalent benzene ring) n expresses the integral value of 1-3)

[0010] The compound shown by this the [-izing 1] is used as a raw material of a sol and a gelation reaction with the compound of the structure generally shown by the following [-izing 2], although it is usable even when it is independent.

[0011]

[Formula 2]



the inside of a formula, and R -- ** -- CH3 and ** C2 H5 etc. -- an alkyl group is expressed namely, a group by which the compound shown in (** 2) is generally called tetrapod alkoxysilane -- the compound is shown

[0012] The spherical aggregate of the structure shown in (** 3) by the technique shown in the following examples is prepared using such a raw material. However, it is an example about the method of preparation, and it is the spherule which was obtained by the method of preparation of other spherules, and the following can be used for this application as a **** column packing material, when it has nature [of organic] joint Q. Hereafter, the characteristic feature of this invention is described, explaining the concrete mode in instantiation.

[0013]

[Example 1]

(Adjustment of a raw material)

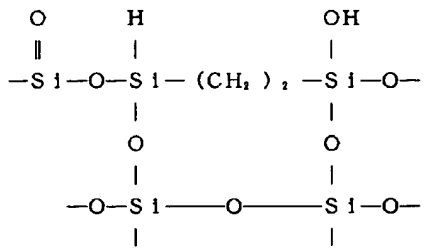
(The first process) the compound (R'=C2 H5, Q= (CH2) 2, and M=Si) shown in this at (** 1) after making the ethanol solution of a tetrapod ethoxy silane (component equivalent to TEOS, an abbreviated name, and the [-izing 2]), and a hydrochloric-acid acid ethanol solution react at mixture and a room temperature for 1 hour -- adding -- further -- it is made to react for 1 hour

[0014] (The second process) The reaction mixture of the 1st above-mentioned process is added in the ammonia basic ethanol aqueous solution, and also stirring is performed for 2 hours. By choosing conditions, such as the shape of a stirring wing shape, and a rotational frequency, the reaction mixture of the 1st process is torn off by the shearing force by the stirring airfoil, the half-solidification [carrying out a balling up and both, drifting in a reaction mother liquor, with the boundary tension of oneself,] by which fine-grain liquefaction is carried out according to a sol and a gelation reaction gradually advances in a reaction mother liquor, and the water gel near a true sphere is obtained. Since gelation is progressing even if it carries out this object a ** exception from a mother liquor, the shape of a sphere does not collapse. A spherical diameter is experientially controlled by the shape of a stirring wing shape, and the rotational frequency.

[0015] (The third process) Only the skeleton which the water gel obtained according to the above-mentioned process becomes from the component which moisture evaporates by xeransis and is shown in [-izing 3] remains, and the porous material object near a true sphere is obtained. By the sieve method, this compost can be sorted out to the particle size distribution suitable for the column packing material, and can be ****ed as a bulking agent. In addition, it is necessary to choose xeransis conditions, discerning the performance as a bulking agent, since the adsorption moisture which remains in a minute amount on the thing for which it has the nature combination (Q) of organic in the skeleton, and the front face of a bulking agent or H which it is ****ed and is generated, and OH base are delicately related for the performance of a bulking agent. Generally it is chosen out of 50-150 degrees C under an ordinary pressure or reduced pressure.

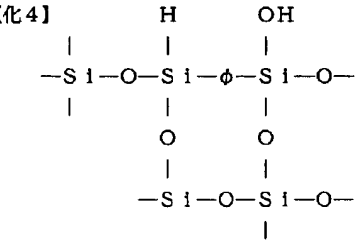
[0016] If the constituent adjusted by the technique of the above [the 1st - the 3rd process] expresses typically, it will be presumed to be what has the structure like following [-ized 3].

[Formula 3]



However, the case where M under [-izing 1] is Si is shown.
[0017] Compared with the conventional silica gel being formed from the configuration of [**Si**O**Si**], namely, the silica gel system constituent shown in [-izing 3] As shown above from the result of various physicochemical measurements, it is **(CH2) n ** or] n between ** Si ** and ** Si ** like the [-izing 4] which carries out a postscript (**phi**). What has the canal component was presumed. With the rate of a raw material compounding ratio shown in the [-izing 1] and the [-izing 2], although the outline control is possible for the fraction which has the [**Si**(CH2) n **Si**] combination in the constituent, and the proportion (r) of [-Si-O-Si-] The modality of dissociated component and the relation with the polarity of an expansion solvent also have a relation with the separability ability at the time of using as the proportion (r) and a bulking agent, and mainly, optimum conditions are chosen experimentally and it is set up.
[0018] In addition, as Q under [-izing 1], a methylene group (n= 1) besides the ethylene of [-izing 3], a trimethylene machine (n= 3), a propenyl machine (n= 3), etc. can be illustrated as a divalent chain compound. For example, 1, 2-bis(triethoxy and silyl) ethane(product made from Shin-etsu chemistry);1, and 2-bis(triethoxysilyl) methane; etc. can illustrate concretely. This etc. is compounded commercial elegance or himself and is used.
[0019] (The 4th process) The embellishing method (A)
The spherical object aggregate obtained at the 3rd process can be used by the ability filling up the ** ********. However, processing the front face of this spherical particle in other chemistry articles, and reforming the separability ability of a column packing material (modification manipulation) is performed if needed. For example, it is the above (**Si**O**Si**), and (**Si**(CH2) 2 **Si**) as an example in the case of the spherical particle of a system, by making it react with an octadecyl dimethyl chlorosilicane, the property can be embellished and it can be used now as the so-called antiphase system (ODS type) bulking agent.
[0020] (Process schematic drawing) When the content of the explanation about the above 1st - the 4th process is typically shown in a schematic diagram, it is as being shown in drawing 1 .
[0021]
[Example 2]
(The 1st process) By the same technique as the above (example 1), react by addition, the inside of the hydrochloric-acid acid aqueous solution and ethanol are made for a compound [-izing 1] and a compound [-izing 2] to react preparatorily with a sol-gel method in ordinary temperature further for 2 hours, and oligomer is compounded as a precursor.
[0022] (The 2nd process) The embellishing method (B)
the inside of the reaction mother liquor which the oligomer obtained at the last process suspends -- a silica gel flour (five to 100 micrometer mean particle diameter) -- an injection -- a gelation reaction is advanced further In this case, adding a supersonic oscillation for 30 minutes, in order to make variance of a silica gel flour good and to improve the contact to oligomer, powerful stirring is continued like an example 1 and a gelation reaction is completed. By such operation, a silica gel fine grain can be made a nucleus (SiO 2), and the spherical composite which contains [**Si**(CH2 </SUB>) 2 **Si**] in a cortex component can be obtained. Future processing was made to be the same as that of an example 1.
[0023]
[Example 3] In the compound shown in the general formula [-izing 1] in an example 1, the operation except having used the compound which has a phenylene group as a raw material obtained the spherule set object as a cyclic compound in which Q has a divalent residual valence like the technique (he has no 4th process; modification processing) shown in an example 1 and the processes 1-3, and abbreviation.
[0024] If the constituent adjusted by such technique is expressed typically, what has the structure like following [-ized 4] will be presumed.

【化4】



However, for Si and Q, phenylene-group and R' is [M under [-izing 1]] CH3. The case where it is a machine is shown.

[0025] in addition -- Q shown in the [-izing 1] which is a raw material ****** -- except for the phenylene group (**phi**) of the above-mentioned example -- or (**phi**phi**) a benzylidene machine, a styryl machine, etc. which have a free radical in a side chain can also include a divalent ring compound into the component of a gel-like spherule by the same technique For example, 1, 4bis (triethoxysilyl), bemzene;9, 10-bis(triethoxysilyi) anthracene;4, and 4'-bis(triethoxysilyl) biphenyl etc. can illustrate concretely.
[0026]
[Example 4]
[The example 1 of a comparison] (Alkali-proof sex test)
(Adjustment of a sample) The sample offering sample was adjusted by the place method shown above (example 1). However, the compounding ratio was made into the [-izing 1] / [-ized 3]=0.05(weight ratio:%) ** (r). If r exceeds 0.15%, the rigidity of the obtained gel becomes small and will be in the soft status. There are few the addition effects 0.02 or less, and it was thought in the result which is a trial production that the r= 0.05 neighborhood was suitable as physical physical properties of a spherule.
[0027] (An alkali resistant test and result) The sample offering sample was ground, respectively and the amount of 25 degrees C and 6 hour immersing; ****** was measured by the weight method to 1N ** NaOH. A test result is shown in [Table 1].
[Table 1]

	供試　試料	溶残物重量
比較例１	市販品シリカゲル	０％
実施例４	実施例１の処法による調製品	２０％

[0028] (View) In order to compare alkali resistance, it examined in the lye deeper than general analysis conditions. SiO2 Although it melted by the lye completely in the case of the commercial silica gel which consists only of a component and there was no survival, a survival accepts and the sample which introduced the hydrophobic group shows that alkali resistance became good relatively.
[0029]
[Example 5] (Observation of the spherical nature of a bulking agent)
1. The configuration was observed for the set object for bulking agents obtained according to the sample offering sample; example 1 (processes 1-3) using the scanning electron microscope.
2. An observation result is shown in drawing 2 (photograph copy). However, A (sample of an example 1) and B (sample of an example 3) are shown, respectively. It turns out that the grain for bulking agents is the true sphere-like set object with which what ** also became independent.
3. The commercial silica gel (letter of spallation) of the view; former has the large aspect ratio of grain, the restoration nonuniformity to a column arises, and although the repeatability in an analysis value was low, grain has suggested near and the repeatability with good uniform restoration and measured value to the true sphere (aspect ratio 1).
[0030]
[Example 6]
[The example 2 of a comparison]
(Physical-properties value measurement result of a bulking agent)
1. It prepared by the technique described in the example 1 of the sample; above offered as a sample. The silica gel used for the example 1 of a comparison ground commercial elegance, arranged grain size and used it.
2. The following performed the physical-properties measuring method.
(1) Grain size and particle size distribution: It is based on the copy image analyzer of a scanning-electron-microscope (SEM) observation photograph.
(2) Specific surface area : BET adsorption method (N2 : multipoint method)
Use device microphone ****** tex ******** 2400 predrying 80 degrees C 3hr degasifying processing Reduced pressure 100 degrees C, 3hr(3) pore distribution : N2 Gas-absorption-method use device ********** tex ******** 2400 predrying 80 degrees C 3hr degasifying processing Reduced pressure 1000 degrees C, 3hr[0031]

	充填剤	平均粒径（μm）	平均細孔径Å	比表面積（m^2/g）
実施例６	実施例１の方法で調製	１０．２	２０４	４３０
比較例２	SiO_2	１０．５	１４８	３２０

[Table 1] The physical-properties value of a bulking agent

[0032]

[Example 7]
(Authentication 1 of a hydrophobic-group introduction)
1. Grind the spherical particle prepared by the technique described in the example 1 of the sample:above offered as a sample, and it is it a top and about 500kg [/cm] lower twist by restoration and punch to a cylindrical shape-like die 2 The pressure was put, the disk of 0.15mm ** and the diameter of 20mm was made, the infrared (IR) spectrophotometer was equipped with this, and the extinction status of the transmitted light was measured.
[0033] 2. The measurement result for every wavelength of IR (KBr) transmitted light in measurement result:R=CH3 CH2-;Q=-CH2 and CH2- is shown in drawing 3 . ** ** ****** was checked to 2980 and C'-H expansion and contraction aliphatic in 2970 or 2950/cm so that it might see in this drawing. Presence of -CH2-CH2- was checked in accordance with the numeric value this is indicated to be to reference.
[0034]
[Example 8]
(Authentication 2 of a hydrophobic-group introduction)
1. The sample plate was prepared by the technique by the example 7 using the spherical particle prepared by the technique described in the example 3 of the sample:above offered as a sample.
[0035] 2. Measurement in R=CH3 CH2-;Q=-phi- was performed by the same technique as a measurement result:precedent. In this case, ** ** ****** was observed to CH expansion and contraction aromatic near 3060/cm, and the reference value was in agreement. Thereby, presence of the benzene ring (-phi-) was checked in the sample offering sample.
[0036]
[Example 9]
(1) It is Detection : Shown [UV254 nm sample-offering Sample :] in mixed liquor (3) separation result view 5 of a pyridine (1 in drawing), and phenol (2) by using spherical grain set object obtained according to example 1 (processes 1-4) as column packing material (fixed bed) instantiation (2) experiment condition column room temperature, and 1ml/. : 4mm bore moving bed : The acetonitrile / 0.01 mol and phosphate buffer solution =1/1 rate of flow : Quadrature-axis T shows the signal strength relevant to [in axis-of-ordinate H] the amount of detections for the elapsed time of the time of sample injection, and it is shown that separability ability is good.
[0037]
[Example 10]
(1) It is the same as that of the instantiation (2) experiment conditions (example 9) using the spherical grain set object obtained in the example 3 as a column packing material (fixed bed).
(3) It is shown in separation result view 6. The method of presentation is the same as that of (an example 9). Having good separability ability is shown.
[0038]
[Effect of the Invention] The place characterized [especially / the] by this invention about the new column packing material for liquid chromatography is spherical object aggregate which uses the specific alkoxide silane compound (** 1) which has the nature combination (for example, hydrophobic group) of organic as a constituent, uses as a raw material the object which mixed the tetrapod alkoxide silane compound this and if needed, and is compounded with a sol-gel method as a raw material used in case of the manufacture. By using such a specific raw material, the canal fraction (**Si**Q**Si**) which comes to the front face from a raw material exists, and the manufactured bulking agent discovers the unique separability ability different from the bulking agent which consists of the ability to set as (**Si**O**Si**) to the conventional commercial silica gel.

[Translation done.]